

III. AMENDMENTS TO THE SPECIFICATION

On page 2, please **amend** the paragraph beginning on line 6 and ending on line 18 as follows:

a³ The three dimensional structure of a target protein may not be known experimentally. In these situations, a database of knowledge may be available for the target protein which correlates the activity of a given ligand with variations in its structure. This is commonly known as a structure-activity relationship, (SAR). There are many molecular parameters that can be considered a part of an SAR including surface area, molecular weight, hydrophobicity, and molecular field. Metrics which describe some combination of these parameters can be correlated to desired biological activity. Subsequently, extrapolations beyond the initial SAR test set of molecules can lead to the discovery of new chemical entities. See FY Wiselogle, ed. A Survey of Antimalarial Drugs, Ann Arbor: JW Edwards, 1946; PB Marshall; *Some chemical and physical properties associated with histamine antagonism*; Br. J. Pharmacol. 10: 270- 280, 1955; RP Stephenson, *A modification of receptor theory*, Br. J. Pharmacol. 11:379-384, 1965; and McConnell HM, Owicki JC, Parce JW, Miller DL, Baxter GT, Wada HG, Pitchford S., *The cytosensor microphysiometer: biological applications of silicon technology*, Science 257:1906-12, 1992, hereby incorporated by reference.

On page 46, please **amend** the paragraph beginning on line 7 and ending on line 20 as follows:

a⁴ Using comparative antibody affinities for test compounds and measured IC₅₀ values, the monoclonal antibodies can be used to model the PDEIV binding site itself, and to predict structures of additional PDEIV inhibitors. For example, the IC₅₀ for Compound A is 410nM, while the IC₅₀ for Compound C is 800nM and for rolipram the IC₅₀ is 3000nM. Additional examples of PDEIV inhibiting compounds can be included in this database and are exemplified in co-pending U.S. Patent Application Serial No. 08/647,419, filed May 9, 1996, abandoned,

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U.S. Patent Application Serial No. 08/782,502, filed January 10, 1997, now U.S. Patent No. 5,922,751, U.S. Patent Application Serial No. 08/875,487, filed July 8, 1997, now U.S. Patent No. 6,153,630, U.S. Patent Application Serial No. 08/659,767, filed June 6, 1996, now U.S. Patent No. 5,864,037, U.S. Patent Application Serial No. 08/714,581, filed September 16, 1996, now U.S. Patent No. 5,744,473, U.S. Patent Application Serial No. 08/833,893, filed April 10, 1997, now U.S. Patent No. 6,075,016, U.S. Patent Application Serial No. 08/860,680, filed June 11, 1997, now U.S. Patent No. 6,066,641, U.S. Patent Application Serial No. 08/860,674, filed June 11, 1997, now U.S. Patent No. 6,025,361, U.S. Patent Application Serial No. 08/151,949, filed September 11, 1998, now U.S. Patent No. 6,372,720 and U.S. Patent Application Serial No. 08/963,054, filed November 11, 1997, now U.S. Patent No. 6,166,041, the disclosures of which are all incorporated by reference herein in their entirety.
